

Personal

April 24, 1974

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Dear Jerry:

Plans seem to be crystalizing so that I shall be arriving at your house by automobile late in the afternoon of Saturday, May 4. Eleanor and I are delighted with your proposal that we visit you that evening, make a half-hour recording as you propose, and depart the following morning to Greeley to visit my son and his wife and in-laws, in-laws whom we have not yet met.

As to the content of the half-hour tape recording, the high spots would be somewhat as follows.

In the three or four months after the termination of World War II, Dr. Maurice Visscher and Dr. Owen Wangensteen, jointly hatched the idea that the project of developing a heart-lung machine be proposed to me as a major investigative project.

The idea sounded fascinating, and I started to make inquiries around the country to learn whether anyone else had worked in this area. In the course of a ten-day trip including the meeting of the Society of University Surgeons in New York in February of 1946, I had a conversation with Dr. Edward D. Churchill at the Massachusetts General Hospital. Dr. Churchill immediately pointed out that Dr. John H. Gibbon had been working on precisely this project, starting approximately 1934 or 1935. Jack Gibbon was just back from military service and had taken up his new position at Jefferson Medical School in Philadelphia. Later on the same trip, therefore, I stopped in to see him and his associates. His equipment from Massachusetts General was still crated and he had very little to show me actually in hand. we exchanged ideas verbally, and he expressed immense appreciation that somebody else was becoming interested in this project besides himself and his wife Maly.

Funds were sought to pursue this work. Initially, for reasons which I do not now recall, efforts were made to obtain research money from

The United States Navy. This agency consumed almost a full year in reviewing the situation, then reported that it vigorously approved it but that it had no money to support the research. An effort was therefore made to obtain funding from the National Institutes of Health. This effort was successful, and funding began in July 1947. I was joined in the laboratory by Dr. Karl E. Karlson, now at the University of Rhode Island, and we set up equipment patterned after Willem Kolff's initial artificial kidney, inasmuch as during an earlier visit to Minnesota Kolff had indicated that oxygenation of the blood took place in the course of passage through that artificial kidney. The following year the grant was renewed, now under the aegis of the newly established National Heart Institute, 10% of the funds of which were applied to this particular project that first period, namely the sum of \$14,500.

Various devices were developed and evaluated. We had visits back and forth between Philadelphia and Minneapolis on several occasions, and there was a general understanding with Jack Gibbon that our information would be pooled in order to make the most of it no matter which laboratory was the more productive. In 1949 Gibbon appeared to be becoming somewhat discouraged. He made a trip to Minneapolis and talked before the Minneapolis Surgical Society. During that visit he inspected what our group was doing in the laboratory and came to the conclusion that the pooling of information from the two laboratories suggested the continued feasibility of the project and went ahead with renewed vigor which ultimately, as you know, was successful.

Our own group in Minneapolis was ready for clinical applications in the spring of 1951, with a revolving screen oxygenator. Dr. Richard Varco was enlisted into our group after we had successfully opened and closed the atria on 30 dogs in succession. In the last couple of these Varco participated. The first patient had had an earlier exploration for a supposed mitral stenosis. When none was found and a defect between the atria was recognized by the exploring finger, the patient's wounds were closed, and the patient was put on the waiting list until the machine should become available. Re-exploration was performed on April 5, 1951. The physiological performance of the pump-oxygenator was gratifying and highly successful, except that flows through the extracorporeal system were controlled on the basis of mean oxygen saturation using the refined oximeter devised by Earl Wood and his group at the University of Minnesota. Unfortunately, in the presence of heparinization there was interstitial hemorrhage into the lobe of the ear, giving the impression of marked desaturation. We therefore ran flows higher than 200 ml per kilogram per minute during most of the perfusion. Unfortunately, the patient's lesion proved to be a patent atrio-ventricular canal, which defied our efforts at either recognition or correction.

A second patient was explored about three weeks later. This patient proved to have a straightforward interatrial septal defect. The catastrophic outcome resulted from the failure of the operator of the pump-oxygenator to turn on the switch powering the level-control mechanism upon which we had all worked for twelve months in preparation.

The decision had already been made at this time that Dr. Karlson and I and 5 of our team should move to the State University of New York in Brooklyn during the late summer of 1951. We were greatly encouraged in making this move by the presence of a pediatric cardiologist with 160 patients in reserve and by the presence of an adult cardiologist who enthusiastically offered to give us support. Unhappily, following our arrival in Brooklyn one of these men declined to give us support unless we could guarantee the safe survival of the patients in question, and the other found he could not give it the needed time. It was therefore not until the summer of 1955 that, using essentially the same equipment which we had brought along from Minnesota, we had an operable patient upon whom to work, with a highly successful outcome. By this time, of course, Jack Gibbon had been successful with his first patient, in 1953. It is gratifying that he elected to report this accomplishment in Minnesota Medicine.

Other avenues of investigation were therefore explored. In 1955, a group of us, including Melvin Newman, Karlson, and Jackson Stuckey, provided partial cardio-pulmonary bypass for a short series of patients with irreversible chronic heart failure. There was striking clinical improvement in each, with loss of edema and good diuresis. Inasmuch as the combined valvular lesions could not be satisfactorily attacked at this time, the improvement was temporary. For instance, one of these patients died in an ambulance on the way to another hospital a month after perfusion when the ambulance attendant insisted that she lie down rather than sit up.

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Having had this experience, we looked for patients who might be benefitted in the long run and it occurred to me that the patient with acute myocardial infarction and shock might very well recover if he could be carried over the acute episode. A series of four patients with the diagnosis of myocardial infarction and shock was supported in this fashion. Unhappily one of these proved to have been misdiagnosed and turned out to have purulent peri-carditis. That patient was obviously not improved at all by perfusion and died in short order. The other three patients survived partial cardio-pulmonary bypass for several hours. The first of them made a long painful recovery but is still alive and still operating his

clothing store in Brooklyn, seventeen years later. The second patient did nicely for several days and died upon sudden exertion in the middle of the night while not under close supervision. The third patient died about a day and a half after perfusion with extension of his myocardial infarction, found to involve the entire left ventricle at autopsy.

We were criticized by several workers on the basis of the work of Peter Salisbury and of Sarnoff and Braunwald. The latter had done work suggesting that the pressure against which the left ventricle empties is the major determinant of the amount of work which it must do. Inasmuch as we had not reduced that pressure, it was their thesis that this approach had very little likelihood of providing help to the sick heart.

With this problem in mind, I took a year of sabbatical leave in order to work with Ake Senning and Clarence Crafoord at the Karolinska Institute, from 1960 to 1961. During the course of this year it was possible to prove conclusively that the work of the left ventricle can be cut approximately in half by diversion of the blood from the left atrium to the aorta, to which it is returned continuously under pressure, without reduction in the mean aortic blood pressure. Armed with this information, the group of us in Stockholm devised a cannula and a technique permitting us to perform left ventricular bypass without opening the chest. We sought applications of this beyond our physiologic investigations in animals and utilized it in a series of some 25 patients. No patients with myocardial infarction and shock were long-term survivors, although two or three of them recovered enough to have the cannula removed, only to die within a day or two. There were four cases, handled by Dr. Richard Campellatti after his departure from Downstate but included among the 25 which, represented survivals. Three of these had chronic left heart failure in combination with abdominal emergencies requiring exploration. They were considered by the cardiologists to have sufficient cardiac insufficiency to make the exploration under ordinary circumstances prohibitively risky. They recovered following performance of abdominal exploration in the presence of left heart bypass and left the hospital in satisfactory condition. A fourth patient with acute left heart failure but without myocardial infarction also survived following about two hours of left heart bypass.

The procedure of left heart bypass for myocardial infarction was not continued because the natural suspicion of the cardiologists was such as to make them fearful of what they regarded as a swordswallowing type of performance. The last two patients were referred to us for possible bypass only after all electroencephalographic activity had

disappeared. When this point was protested, it was pointed out that our mortality had been so high that they felt that it was not appropriate to transfer them until death otherwise was inevitable. In view of the development and popularization of intra-aortic balloon pumping by Adrian Kantrowitz, also in our department of surgery in Brooklyn, it is probable that we could go back at the present time to left heart bypass. The amount of manipulation necessary however, is considerably larger than to use straightforward cardio-pulmonary bypass on a temporary basis, especially now that membrane oxygenators are available for that purpose.

I take considerable pride in the work which was done in the laboratory at Downstate, much of it without my own personal contribution at all. An example of this is the method of electrical identification of the bundle of His during open-heart operations, developed by Jackson H. Stuckey and Bryan Hoffman. This was utilized on a small series of patients with great success in Brooklyn, but the flow of patients was not large enough to be convincing.

At the present time, Dr. James Malm and his associates, now including Dr. Bryan Hoffman, Mr. Samuel Rossy and others of the group formerly at Downstate, are utilizing this method on a larger series of patients in order to evaluate the importance thereof. In complicated procedures it appears to be very important, indeed essential

Another development within our own laboratory was external compression counterpulsation. I worked on this for two years or more, obtained a patent on it thru NIH, and demonstrated that it was as effective as straightforward counterpulsation in the dog, but dropped it because of the conviction that sufficient vascular disease to embarrass the myocardium would also interfere with the pliability of the peripheral vessels and thereby interfere with the effectiveness of the method. It would appear today that others, such as Dr. Harry Sorooff, with perhaps considerably more ingenuity than I demonstrated, will succeed in making this mechanism of support feasible. Time will tell.

Another contribution which developed out of the arena of work on the pump-oxygenator was that of Russell M. Nelson in discovering the role of Gram-negative endotoxin in shock, well ahead of Fine and Frank but an amplification of the much earlier work of J.C. Aub.

Still another contribution from this group was the development of a prosthetic ball valve for replacement of the natural mitral valve of the dog, the longest survivor coming to grief after 3 months of renal emboli. Albert Starr makes generous recognition of this in his first report, 5 years later, of success if anticoagulants are used chronically.

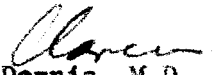
Finally, the contributions of Sobol, Kaplitt, and Sawyer in development of the techniques of gas endarterectomy were a source of real gratification.

Laboratory and clinical investigative groups occasionally gain sufficient momentum to be almost self-sustaining. To watch a group containing the people already noted and many others from medical students to senior faculty, from technicians to senior physiologists, engineers, and chemists, has been one of the most rewarding aspects of my academic career. Almost every one of them contributed with enthusiasm, and I wish to be recorded in expressing my gratitude to them.

Perhaps this is too detailed or too long, but it outlines in general what it seems to me might be covered in such a tape recording as you propose.

Eleanor and I look forward to our visit with you and wish to express our appreciation for your kind invitation.

Very sincerely yours,


Clarence Dennis, M.D., Ph.D.
Special Assistant for Technology
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NHLI:CDennis:mmh